

Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (Currently Amended). A pharmaceutical composition for modulating at least one inflammatory response associated with human heparin binding protein (hHBP), said composition comprising ~~an a monoclonal antibody against which binds~~ hHBP (SEQ ID NO: 1) or a compound comprising an hHBP-binding fragment of said antibody, ~~or an antibody against a homologue of hHBP or a fragment of said antibody,~~ wherein the antibody or compound ~~(i) is capable of binding to an epitope within the sequence consisting of amino acid residues 1 to 19 or 45 to 226 according to SEQ ID NO: 1 and thereby stimulating at least one inflammatory response associated with hHBP, or (ii) is capable of binding to an epitope within the sequence~~ hHBP (20-44) consisting of amino acid residues 20 to 44 according to SEQ ID NO: 1 and thereby inhibiting at least one inflammatory response associated with hHBP,

wherein said antibody or compound is capable of reducing IL-6 levels in whole blood attributable to exposure to hGBP (20-44) and a bacterial product by at least about 6 fold.

2-5 (Cancelled).

6 (Previously Presented). The pharmaceutical composition according to claim 1, wherein the antibody is produced by a cell of clone F19A5B4 (ECACC Ass. No.: 03090302).

7 (Previously Presented). The pharmaceutical composition according to claim 1, wherein the antibody is a polyclonal antibody.

8 (Withdrawn). The pharmaceutical composition according to claim 1, wherein the HBP homologue is porcine heparin binding protein (pHBP) (SEQ ID NO: 588).

9 (Withdrawn). The pharmaceutical composition according to claim 1, wherein the HBP homologue is human neutrophil elastase

(hNEL) (SEQ ID NO: 589).

10 (Previously Presented). The pharmaceutical composition according to claim 1, wherein the modulating of at least one inflammatory response being

- i) up- or down regulating the gene expression in the immune cells, preferably monocytes/macrophages, leading to secretion of endogenous inflammatory mediators including receptors for inflammatory mediators and transcription factors involved in the signal transduction of the inflammatory mediators, activation of the production of bradykinin by the phase contact system, and/or
- ii) increasing or decreasing the blood concentration of monocytes and/or local accumulation thereof at the sites of inflammation, and/or
- iii) increasing or decreasing the life-time of monocytes, neutrophils and other immune cells due to inhibition of apoptosis, and/or
- iv) activating or inhibiting the expression of adhesion molecules by the vascular endothelial cells, and/or
- v) activating or inhibiting the contact phase system producing bradykinin leading to an increased vascular permeability, and/or
- vi) increasing the phagocytic potential of monocytes/macrophages, and/or
- vii) up-regulation of class-II MHC.

11 (Original). The pharmaceutical composition according to claim 10, wherein the immune cells are monocytes/macrophages.

12 (Previously Presented). The pharmaceutical composition according to claim 10, wherein the mediators are cytokines, selected from the group consisting of TNFalpha, IL-1, IL-6, G-CSF, GM-CSF, and M-CSF, chemokines selected from the group consisting of IL-8 and MCP-1, or receptors selected from the group consisting of Tissue factor and IL-2Ralpha.

13 (Original). The pharmaceutical composition according to

claim 10, wherein the adhesion molecules are selected from the group comprising PECAM, ICAM-1, E-selectins and VCAM-1.

14 (Withdrawn). The pharmaceutical composition according to claim 10, wherein the antibody is a pro-inflammatory antibody capable of stimulating the at least one such inflammatory response in the absence of bacterial products in the blood.

15 (Withdrawn). The pharmaceutical composition according to claim 10 wherein the antibody is a pro-inflammatory antibody capable of stimulating the at least one such inflammatory response in synergistic action with bacterial products present in the blood.

16 (Withdrawn). The pharmaceutical composition according to claim 10, wherein the antibody is capable of stimulating the synthesis and/or release of cytokine IL-6.

17. (Cancelled)

18 (Previously Presented). The pharmaceutical composition according to claim 10, wherein the antibody is an anti-inflammatory antibody capable of inhibiting the at least one such inflammatory response in the absence of bacterial products in the blood.

19 (Currently Amended). The pharmaceutical composition according to claim 10, wherein the antibody is an anti-inflammatory antibody capable of inhibiting the at least one such inflammatory response ~~as defined in claims 10-13~~ in the presence of bacterial products in the blood.

20. (Cancelled)

21 (Withdrawn). The pharmaceutical composition according to claim 15, wherein the bacterial products are selected from the group consisting of LPS (Lipopolysaccharide), PGN (peptidoglycan), LTA (Lipotechoic acid), MDP (muramyldipeptide) and PCW (purified cell wall from bacteria).

22-23 (Cancelled).

24 (Previously Presented). An hHBP binding anti-inflammatory monoclonal antibody having all of the identifying characteristics of the monoclonal antibody produced

by clone F19A5B4 (ECACC 03090302), or an antibody fragment which is an hHBP-binding fragment of said monoclonal antibody.

25 (Cancelled).

26 (Currently Amended). A cell producing the antibody according to claim 22 1.

27-28 (Cancelled).

29 (Currently Amended). A The composition of claim 1, wherein the compound is a recombinant protein ~~comprising the antibody fragment of the antibody of claim 23, said fragment being capable of binding to an epitope within the sequence consisting of amino acid residues 20 to 44 according to SEQ ID NO. 1 and thereby inhibiting at least one inflammatory response.~~

30-43. (Cancelled)

44 (Withdrawn). A method of modulating the inflammatory response in a subject which comprises administering an inflammatory response-modulating amount of a composition according to claim 1.

45-47 (Cancelled).

48 (Withdrawn - Currently Amended). The method of claim ~~46~~ 44, wherein said composition comprises antibody F19A5B4 or a hHBP-binding fragment thereof.

49 (Withdrawn). The method of claim 44, wherein the inflammatory response is a response to bacterial infection.

50 (Withdrawn). The method of claim 49, wherein the infection is a Gram negative bacterial infection.

51 (Withdrawn). The method of claim 49, wherein the infection is a Gram positive bacterial infection.

52 (Withdrawn - Currently Amended). The method of claim ~~46~~ 44, wherein the inflammatory response is associated with sepsis, severe sepsis, sepsis shock and/or disseminated intravascular coagulation.

53 (Withdrawn). The method of claim 44, wherein the inflammatory response is associated with meningitis.

54 (Withdrawn). The method of claim 53, wherein the meningitis is meningococcal meningitis.

55 (Withdrawn). The method according to claim 51, wherein the infection is by *Pneumococcus pneumoniae*.

56 (Cancelled).

57 (Withdrawn). A method for treating individuals having a sustained inflammatory response comprising administering an effective amount of antibody F19A5B4.

58 (New). The composition of claim 1, wherein said bacterial product is PGN.

59 (New). The composition of claim 1, wherein said antibody or compound is capable of reducing IL-6 levels in whole blood attributable to exposure to hHBP (20-44), in absence of a bacterial product, by at least about 15%.

60 (New). The composition of claim 1, wherein said antibody or compound is capable of reducing IL-6 levels in whole blood attributable to exposure to hHBP (20-44), in absence of PGN, by at least about 15%.